REMARKS

Claims 1-8, 10-12, 14-16 and 18-27 are pending in the above-identified patent application. Claims 1, 7, 10, 14, 16, 18, 20 and 21are amended herein. Claims 9, 13 and 17 are canceled. Claims 22 and 24-27 are withdrawn. No new matter is introduced.

1. Restriction

Applicants have amended dependent claims 7 and 18 to delete non-elected subject matter.

2. Claim Objections

The Examiner objected to claims 11 and 14 for (respectively) omission of the word "or" and omission of a period. Applicants apologize for these errors and have amended claims 11 and 14 to make the appropriate corrections.

3. Claim Rejections Under 35 USC §102

The Examiner rejected claims 1-20 and 23 under 35 USC §102(b) as being anticipated by Macor et al, WO 96/03400.

The Applicants respectfully disagree with the Examiner. A genus does not always anticipate a claim to a species within the genus. When the compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g., select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated. *Ex parte A,* 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990) (MPEP §2131.02).

WO 96/03400 does not disclose any specific compounds that fall within the formula of Applicants claim 1. Applicants note that WO 96/03400 discloses a very broad generic formula in which R^2 and R^3 (using the variables of WO 96/03400) may be one of 15 values, including inter alia, $-SO_nR^6$ where R^6 may in turn be one of seven values which include aryl and heteroaryl. However, WO 96/03400 discloses no compounds in

which R^2 is arylsulfonyl as specifically claimed by Applicants. Applicants further note that WO 96/03400 discloses indole-1-benzenesulfonyl compounds (where R^4 is benzenesulfonyl) in Examples 9 (p. 42-45) and Example 11 (p. 46-48). Applicants claims however are limited to 2-benzenesulfonyl indoles and the compounds of WO 96/03400 do not fall within the scope of Applicants claims. Applicants' claimed species cannot be clearly envisaged from the broad generic scope of WO 96/03400 in the absence of specific examples.

Accordingly, Applicants believe that claims 1-20 and 23 are not anticipated by WO 96/03400.

4. Claim Rejections Under 35 USC §103

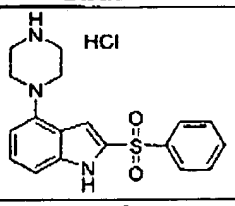
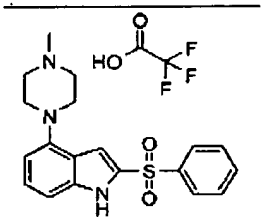
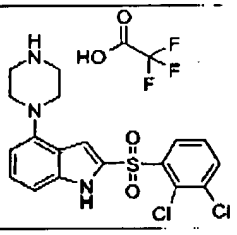
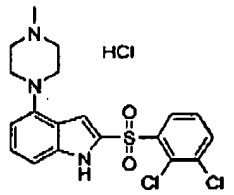
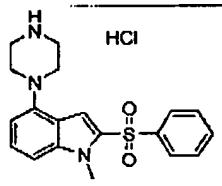
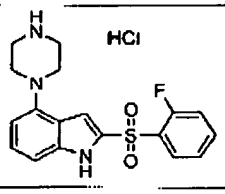
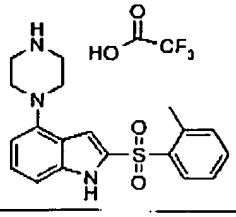
The Examiner rejected claims 1-20 and 23 under 35 USC §102(b) as being anticipated by Macor et al, WO 96/03400. The Examiner stated that it would have been obvious to one having ordinary skill in the art at the time of invention to select any of the species in the genus taught by the reference, including those claimed by Applicants, because the skilled cemist would have the reasonable expectation that ny of the species of the genus would have similar properties.

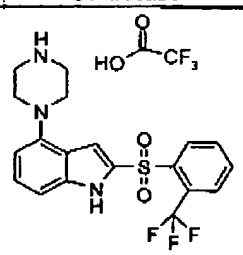
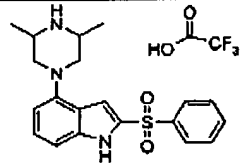
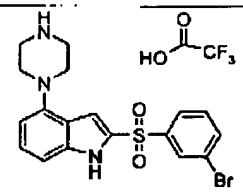
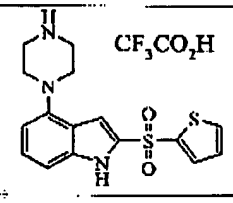
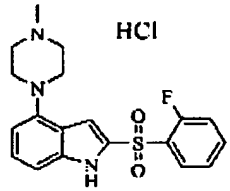
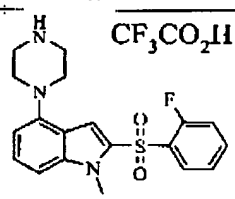
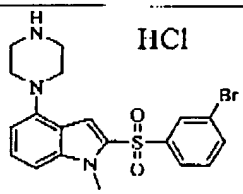
Applicants respectfully disagree. The compounds of WO 96/03400 are reported as being being modulators of the 5-HT1A and 5-HT1D receptors (p. 1-2, 20, 23), and no mention is made of modulation of the 5-HT6 receptor as disclosed in Applicants' specification. Skilled persons do not look to teachings about 5-HT1A and 5-HT1D receptor inhibitors when designing compounds that inhibit different receptors such as 5-HT6.

Applicants believe that the instantly claimed compounds are surprisingly and unexpectedly better inhibitors of the 5-HT6 receptor than those disclosed by WO 96/03400. Table 1 below lists pKi values (determined using the procedure of Example 5 of Applicants' specification) for compounds of Applicants' invention.

Table 1

#	Structure		pKi

#	Structure		pKi
1		2-Benzenesulfonyl-4-piperazin-1-yl-1H-indole	9.9
2		2-Benzenesulfonyl-4-(4-methyl-piperazin-1-yl)-1H-indole	9.9
3		2-(2,3-Dichloro-benzenesulfonyl)-4-piperazin-1-yl-1H-indole	10
4		2-(2,3-Dichloro-benzenesulfonyl)-4-(4-methyl-piperazin-1-yl)-1H-indole	10.2
5		2-Benzenesulfonyl-1-methyl-4-piperazin-1-yl-1H-indole	9.7
6		2-(2-Fluoro-benzenesulfonyl)-4-piperazin-1-yl-1H-indole	10.4
7		4-Piperazin-1-yl-2-(toluene-2-sulfonyl)-1H-indole	10.4

#	Structure		pKi
8		4-Piperazin-1-yl-2-(2-trifluoromethyl-benzenesulfonyl)-1H-indole	10.4
9		2-Benzenesulfonyl-4-(3,5-dimethyl-piperazin-1-yl)-1H-indole	9.1
10		2-(3-Bromo-benzenesulfonyl)-4-piperazin-1-yl-1H-indole	10.3
11		4-Piperazin-1-yl-2-(thiophene-2-sulfonyl)-1H-indole	10.1
12		2-(2-Fluoro-benzenesulfonyl)-4-(4-methyl-piperazin-1-yl)-1H-indole	9.9
13		2-(2-Fluoro-benzenesulfonyl)-1-methyl-4-piperazin-1-yl-1H-indole	9.3
14		2-(3-Bromo-benzenesulfonyl)-1-methyl-4-piperazin-1-yl-1H-indole	9.3

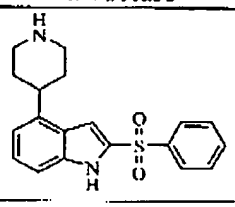
#	Structure		pKi
15		2-Benzenesulfonyl-4-piperidin-4-yl-1H-indole	10.2

Table 1

The generic formula of WO 96/03400 discloses that the variable R^5 may be C_1-C_3 alkylaryl, such as benzyl. The Examiner indicated that skilled persons would have the reasonable expectation that compounds where R^5 is benzyl would have similar activity to Applicants' compounds. However, as can be seen from Table 2, 4-(4-Benzyl-piperazin-1-yl)-1H-indole (compound 1) has a pKi of less than 6 (essentially inactive), more than three orders of magnitude less potent than Applicants' least active compound.

Table 2

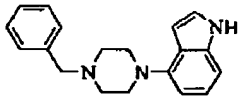
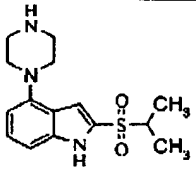
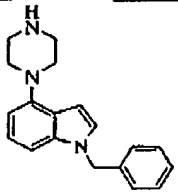
1		4-(4-Benzyl-piperazin-1-yl)-1H-indole	<6
2		4-Piperazin-1-yl-2-(propane-2-sulfonyl)-1H-indole	6.75
3		1-Benzyl-4-piperazin-1-yl-1H-indolee	8.0

Table 2

Compound 2 of Table 2 represents a 2-alkylsulfonyl analog of Applicants claimed 2-benzenesulfonyl compound 1 of Table 1. WO 96/03400 discloses that the variable R^2 may be alkylsulfonyl, and skilled persons again should reasonably expect such compounds to be active. However, 4-piperazin-1-yl-2-(propane-2-sulfonyl)-1H-indole (compound 2, R^2 = isopropylsulfonyl) in Table 2 exhibits a pKi of 6.75, more than two

orders of magnitude lower in affinity than Applicants' least potent compound, and three orders of magintude lower in affinity than the analog compound 1 of Table 1.

WO 96/03400 further discloses that the variable R^4 may be C_1-C_3 alkylaryl, such as benzyl. Compound 3 of Table 2 (where R^4 = benzyl), however, shows a pKi of 8.0, more than an order of magnitude less active than Applicants' weakest compound.

Applicants have narrowed the scope of claims 1, 10, 16, 17 and 21 to delete subject matter that is not directly exemplified by the highly active compounds of Table 1 as submitted herewith. Claims 9, 13 and 17 are canceled for the same reason.

Accordingly, Applicants respectfully submit that Applicants claimed compounds having a 2-arylsulfonyl group show unexpectedly better affinity for 5-HT6 than could reasonably be expected from the teachings of WO 96/03400.

CONCLUSION

In view of the foregoing, Applicants respectfully submit that the claims pending in the above-identified patent application are now in condition for allowance.

Applicants request a one month extension of time for reply pursuant to 37 CFR §1.136(a). Please charge Applicants' deposit account No. 18-1700 for the requisite fee according to 37 CFR §1.17(a)(1).

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-354-7540.

Respectfully submitted,

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